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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Orit Kollet

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09/08/2010

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EXAMINER

KIM, TAEYOON

ART UNIT

PAPER NUMBER

1651

MAIL DATE

DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/552,331	Applicant(s) KOLLET ET AL.	
	Examiner Taeyoon Kim	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 March 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11-74 is/are pending in the application.
- 4a) Of the above claim(s) 11-35 and 47-74 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 36-46 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/3/2010 has been entered.

Applicant's amendment and response filed on 3/3/2010 has been received and entered into the case.

Claims 1-10 are canceled, claims 11-35 and 47-74 have been withdrawn from consideration as being drawn to non-elected subject matter, and Claims 36-46 have been considered on the merits. All arguments have been fully considered.

Applicant's arguments with respect to claims 36-46 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38 and 39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

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art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

The currently amended claims disclose the limitation directed to the method being carried out in the absence of stem cell factor (SCF). The originally filed application does not support this limitation and thus, the instant amendment introduces a new matter to the application.

The current amendment changes the scope of the instant claims. Claim 38 is dependent upon claim 36, and directed to the additional step of exposing the stem cells with a growth factor and/or a cytokine capable of increasing expression of CXCR4.

The specification discloses the administration of HGF alone or HGF in the presence of SCF or IL-6 (p.7 and 33), or the culturing CD34+ stem cells in the presence of HGF alone, or HGF in the presence of SCF (p.36). The scope supported by the original disclosure is considered that the stem cells are exposed to HGF alone, to HGF in the presence of SCF, or to HGF in the presence of IL-6.

Upon the instant amendment, the step (b) of Claim 36 now requires exposing the stem cells with HGF or active portion thereof in the absence of SCF. Claim 38 requires additional exposure step, which is interpreted as independent from the step (b) of claim 36, with the growth factor and/or cytokine. This additional step does not exclude SCF. As a consequence, the method of claim 38 can be interpreted that the stem cells are exposed to HGF in the absence of SCF, which is followed or preceded by the additional exposure step with any growth factor and/or any cytokine, which encompasses SCF. This particular scope does not have support from the original disclosure of the application.

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In amended cases, subject matter not disclosed in the original application is sometimes added and a claim directed thereto. Such a claim is rejected on the ground that it recites elements without support in the original disclosure under 35 U.S.C. 112, first paragraph, *Waldemar Link, GmbH & Co. v. Osteonics Corp.* 32 F.3d 556, 559, 31 USPQ2d 1855, 1857 (Fed. Cir. 1994); *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981). See MPEP § 2163.06 - § 2163.07(b) for a discussion of the relationship of new matter to 35 U.S.C. 112, first paragraph. New matter includes not only the addition of wholly unsupported subject matter, but may also include adding specific percentages or compounds after a broader original disclosure, or even the omission of a step from a method. See MPEP § 608.04 to § 608.04(c). See *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976) and MPEP § 2163.05 for guidance in determining whether the addition of specific percentages or compounds after a broader original disclosure constitutes new matter.

It is recommended to amend the current claims to the step of exposing the stem cells to HGF alone or HGF in the presence of IL-6.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 36-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weimar et al. (of record) in view of Kollet et al. (2001, Blood; of record) in view of in further view of

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Forbes et al. (of record), Devine et al. (of record) and Shi et al. (of record).

Weimar et al. teach a method of exposing CD34⁺ hematopoietic stem cells (HSCs) to HGF and IL-6 (see entire document; Table 2 at p.889).

Weimar et al. do not teach the step of isolating stem cells having CXCR4.

Kollet et al. teach a method of isolating CD34⁺/CD38⁻/CXCR4⁺ HSCs by flow cytometry (FACS) after treating CD34⁺/CD38⁻ or CD34⁺/CD38^{-low} HSCs with IL-6 (see Materials and Methods). Kollet et al. teach that CXCR4 mediates rapid and efficient homing of CD34⁺/CD38⁻ HSCs or CD34⁺/CD38^{-low} HSCs (see whole document).

It would have been obvious for the person of ordinary skill in the art at the time the invention was made to isolate CXCR4 positive stem cells from the CD34⁺ cells treated with HGF and IL-6 taught by Weimar et al.

The skilled artisan would have been motivated to make such a modification because Kollet et al. teach that IL-6 treatment, which increases CXCR4 expression, also increases migration and homing potential (p.3287, right col.), and suggest that the method provides a novel approach to improve the outcome of clinical stem cell transplantation by enhancing homing and repopulation with cytokines (p. 3290), and therefore, a person of ordinary skill in the art would recognize the cells exposed to HGF and IL-6, which inherently express increased CXCR4 would be suitable for transplantation.

The person of ordinary skill in the art would have had a reasonable expectation of success in combining the step of exposing HSCs of Kollet et al. to HGF as taught by Weimar et al.

With regard to the limitations drawn to a method step of expressing HGF in the stem cells, Weimar et al. in view of Kollet et al. do not particularly teach the limitation.

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Forbes et al. teach that HGF as an antifibrotic agent being recombinantly expressed in bone-marrow derived stem cells (p.2, lines 10-13; p.4, lines 18-26).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to use the HGF-expressing stem cells of Forbes et al. in the method of Weimar et al. in view of Kollet et al. or modify the stem cells of Weimar et al. in view of Kollet et al. to express HGF as taught by Forbes et al.

The skilled artisan would have been motivated to make such a modification because using HSCs expressing HGF would eliminate an additional treatment step of HGF, since HGF secreted by the stem cells would act as an autocrine factor for the stem cells.

The person of ordinary skill in the art would have had a reasonable expectation of success in expressing HGF in HSCs since it is well known in the art to generate cells to express recombinant HGF by transfecting a polynucleotide encoding HGF.

With regard to the limitation of claim 37 drawn to the collecting step being effected by a stem cell mobilization procedure, Kollet et al. teach the stem cell mobilization procedure of stimulation with granulocyte colony-stimulating factor followed by obtaining such mobilized stem cells (see Materials and Methods).

With regard to the limitation of claim 46 drawn to a method step of determining homing capabilities of the CXCR4 expressing stem cells, Kollet et al. particularly teach the method step of analyzing homing capability of the stem cells expressing CXCR4 by IL-6 stimulation (see "homing assay" in p.3284, right col.).

With regard to the limitation to the stem cells being mesenchymal stem cells, it would have been obvious to a person of ordinary skill in the art that the method of expressing HGF in

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the bone marrow derived stem cells of Forbes et al. would enclose HSCs as well as MSCs.

Therefore, by using the bone marrow-derived stem cells of Forbes et al. in the method of Kollet et al. would inherently carry out isolation of MSCs expressing CXCR4. Since it is well known in the art that MSCs have the homing property as HSCs according to Devine et al. (see whole document), and it is an inherent property of MSCs to express CXCR4 according to Shi et al. (see entire document), a person of ordinary skill in the art would have a reasonable expectation of success in isolating MSCs expressing CXCR4 along with HSCs in bone marrows in the method of Kollet et al. in view of Weimar et al. in further view of Forbes et al.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taeyoon Kim whose telephone number is (571)272-9041. The examiner can normally be reached on 8:00 am - 5:00 pm ET (Mon-Thu).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Taeyoon Kim/

Primary Examiner, Art Unit 1651